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8/21/97

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 15 1997

WARNING LETTER

VIA FEDERAL EXPRESS

Mr. Helmut Zeph
Owner and Managing Director
Helmut Zeph Medizintechnik Gmbh
Obere Hauptstrasse 16-20
78606 Seitingen, Germany

Dear Mr. Zeph:

During an inspection of your firm located in Seitingen, Germany, on June 6-10, 1997, our Investigator determined that your firm manufactures stainless steel surgical and dental instruments. These are devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that your devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practices (GMP) regulations of 1978, as specified in Title 21, Code of Federal Regulations (CFR) Part 820. The 1978 GMP regulation was superseded on June 1, 1997, by the Current Good Manufacturing Practice (CGMP) requirements as set forth in the Quality System Regulation, 21 CFR Part 820. Since the records reviewed during the inspection were dated prior to June 1, 1997, the deficiencies noted during the inspection reference the 1978 GMP requirements, with a cross reference to the new 1997 Quality System Regulation. Your responses to the Investigator's findings, dated June 26, July 8, and August 6, 1997, were also reviewed. Comments on your response follow each deficiency.

1. Failure to establish and implement specification control measures to assure that the design basis for the device is correctly translated into approved specifications, as required by 21 CFR 820.100(a)(1). This would also be a violation of the Quality System Regulation, 21 CFR 820.75(a). For example, the [redacted] process has not been validated to assure the absence of [redacted] on the instruments.

Your response is not adequate. You state that you will prepare and conduct the validation; however, you did not include any documentation to show that [redacted] process has been validated.

2. Failure to have written procedures describing any processing controls necessary to assure conformance to specifications, where deviations from device specifications could occur as a result of the manufacturing process itself, as required by

21 CFR 820.100(b)(1). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(a) and 21 CFR 820.75(b). For example, there are no written [redacted] procedures for the [redacted] intended to remove [redacted] of the instruments.

Your response is not adequate. A new procedure for [redacted] was included with your response that gives instructions for [redacted] The response references an additional form for recording this procedure; however, this form was not included. There was no documentation to show that this new procedure has been fully implemented.

3. Failure to conduct processing control operations in a manner designed to assure that the device conforms to applicable specifications, as required by 21 CFR 820.100(b)(2). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(a). For example:

   a) Devices required to be [redacted] by the [redacted] specifications and the [redacted] requirements were actually [redacted] according to production record numbers [redacted]

Your response is not adequate. You state that [redacted] instead of [redacted] and that you will cross-out [redacted] on the [redacted] and write [redacted] You do not mention validating or changing this specification in the [redacted] nor making a permanent change in the [redacted] Your process operations should be controlled to assure that [redacted] are being followed and required specifications are being met.

   b) [redacted] specifications required by [redacted] were not followed for the [redacted] process according to many production records, including production record numbers [redacted]

Your response is not adequate. You state [redacted] You do not address why the specifications were not being followed, or if the changes went through a change control procedure. No documentation was provided to show that these changes have been made in [redacted]

4. Failure to follow a formal approval procedure for any change in the manufacturing process of a device, as required by 21 CFR 820.100(b)(3). This would also be a violation of the

Quality System Regulation, 21 CFR 820.70(b). For example, the reasons for changes made to some of the [redacted] were not reviewed, approved, and signed by designated individuals.

Your response is not adequate. You state that you have [redacted] You do not address why the changes were made, or if the changes have been validated and approved through an approved change control procedure.

5. Failure to adequately check each production run, lot, or batch for conformance with device specifications prior to release for distribution, as required by 21 CFR 820.160. This would also be a violation of the Quality System Regulation, 21 CFR 820.80(d). For example:

   a) Devices requiring the [redacted] process and tests were released even though production record numbers [redacted] show that [redacted] process occurred.

Your response is not adequate. You state that [redacted] instead of [redacted] You do not mention validating or changing this specification. You do not address controls that are in place to assure that only devices that meet required specifications are released for distribution.

   b) [redacted] specifications required by [redacted] were not followed for the [redacted] process according to many production records, including production record numbers [redacted]

Your response is not adequate. You state [redacted] You do not address why the devices were approved even though the specifications were not being followed.

6. Failure to adequately investigate any failure of a device to meet performance specifications after the device has been released for distribution, as required by 21 CFR 820.162. This would also be a violation of the Quality System Regulation, 21 CFR 820.100. For example, many defective product returns were not [redacted] as shown in the following [redacted]

Your response is not adequate. A procedure entitled [redacted] was included. This procedure does not address [redacted] does not address required documentation if it is decided that an investigation is not needed. Neither does the procedure address [redacted] requirements. You do not address why the returns specified were not investigated or if those returns have been investigated since the inspection.

7. Failure to review, evaluate, and maintain by a formally designated unit all records of written and oral complaints relative to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device, as required by 21 CFR 820.198(a); and failure to maintain a written record of each investigation made, as required by 21 CFR 198(c). This would also be a violation of the Quality System Regulation, 21 CFR 820.198(a), (b), (e)(6), and (e)(7). For example:

   a) The following [redacted] are not documented or referenced in the [redacted]

Your response is adequate. You performed a review of the [redacted] and provided documentation showing training of staff. The procedure entitled [redacted] requires an [redacted] for [redacted] by reference to [redacted]

   b) Customer complaints, suspected causes of failures, and corrective actions are not always documented in [redacted]

Your response is not adequate. The procedures entitled [redacted] and [redacted] provide instructions on [redacted] and staff members involved received training on these procedures. The response states that staff members are to [redacted] however, these procedures do not address documenting [redacted] The response states that [redacted] The [redacted] will then be reviewed at [redacted] Neither the procedures cited nor the response list the required [redacted] to be implemented.

8. Failure of the device master record to include, or refer to the location of, production process specifications including the appropriate equipment specifications, production methods, production procedures, and production environment specifications, as required by 21 CFR 820.181(b). This would also be a violation of the Quality System Regulation, 21 CFR 820.181(b). For example:

   a) There are no written [redacted] procedures for the [redacted] intended to [redacted] of the instruments.

Your response is not adequate. A new procedure for [redacted] was included with your response that gives instructions for [redacted] The response references an additional form for recording this procedure; however, this form was not included. There was no documentation to show that this new procedure has been fully implemented.

   b) The [redacted] specifications for the [redacted] process have not been documented for [redacted]

Your response is not adequate. You stated that the [redacted] specifications would be included in the [redacted] procedure. The procedure for [redacted] contains a table that lists [redacted] requirements. The procedure does not list [redacted] requirements. According to the procedure the [redacted] are [redacted] if needed. There is no requirement that the [redacted] be recorded.

9. Failure to have written procedures for the removal of manufacturing material, used in the manufacturing equipment or the device, to assure the manufacturing material has been removed or limited to a specified amount that does not adversely affect the device's fitness for use, as required by 21 CFR 820.60(d). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(h). For example, there is no [redacted] used during the [redacted] process, where a [redacted] with the [redacted] can increase the risk of [redacted]

Your response is adequate. You included a procedure entitled [redacted] that contains a

10. Failure to maintain a device history record to demonstrate that the device is manufactured in accordance with the device master record, as required by 21 CFR 820.184. This would also be a violation of the Quality System Regulation, 21 CFR 820.184(d). For example:

    a) The completion of each manufacturing operation is not always [redacted] as required, in the following production records: [redacted]

Your response is adequate. You provided documentation showing that the concerned production employees have received training in completing all documentation.

    b) Routine readings and checks for [redacted] have not been documented.

Your response may be adequate. The procedure for [redacted] includes requirements for testing and documenting [redacted] The response did not include the [redacted] showing that the testing is being performed and documented.

    c) [redacted] used for the [redacted] of the devices are not documented or referenced in the device history records.

Your response may be adequate. You stated that you have added the [redacted] to the [redacted] however, you did not include a copy of the new procedure with your response.

11. Failure of the quality assurance program to assure adequate approval or rejection of all in-process and finished devices, as required by 21 CFR 820.20(a)(2). This would also be a violation of the Quality System Regulation, 21 CFR 820.80(d) and (e). For example:

    a) Devices requiring [redacted] process and tests were released even though production record numbers [redacted] that [redacted] process occurred.

Your response is not adequate. You do not address any quality assurance procedures that are in place to assure that specifications in the device master records are met for finished devices.

b) [redacted] specifications required by [redacted] were not followed for the [redacted] process according to many production records, including production record numbers [redacted]

Your response is not adequate. You do not address any quality assurance procedures that are in place to assure that specifications in the device master records are met for in-process devices.

12. Failure of the quality assurance program to identify, recommend, or provide solutions for quality assurance problems and verify the implementation of such solutions, as required by 21 CFR 820.20(a)(3). This would also be a violation of the Quality System Regulation, 21 CFR 820.100 and 21 CFR 820.20(c). For example, many defective product returns were not [redacted] as shown in the following [redacted]

Your response is not adequate. The procedures entitled [redacted] provide instructions on [redacted] however, these procedures do not address documenting [redacted] The Quality Assurance department cannot [redacted] that are not documented. The response states that [redacted] The [redacted] will then be reviewed at [redacted] The procedures cited do not list required [redacted]

13. Failure of the quality assurance program to assure that all quality assurance checks are appropriate and adequate for their purpose and are performed correctly, as required by 21 CFR 820.20(a)(4). This would also be a violation of the Quality System Regulation, 21 CFR 820.20(b)(3). For example, the facility has no equipment for the [redacted] process; however, [redacted] indicate that the devices go through [redacted] processes.

Your response is not adequate. You state that [redacted] however, the quality assurance program permitted [redacted] indicate that the devices were [redacted] You do not address quality assurance checks that are in place to assure that the processing operations, any testing performed, and records created are for processes that you are capable of performing.

14. Failure to retain all required records pertaining to a device for a period of time equivalent to the design and expected life of the device, as required by 21 CFR 820.180(b). This would also be a violation of the Quality System Regulation, 21 CFR 820.180(b). For example, no [redacted] were kept for the following [redacted]

Your response is not adequate. You state that staff members responsible for the [redacted] records were instructed to find the records pertaining to [redacted] No documents were included showing that the records were found. The response does not state that the records were found.

Your response states that the [redacted] is to be placed into the [redacted] After completion a copy of the [redacted] is placed with the [redacted] and both are placed into the [redacted] These instructions are not included in the procedures entitled [redacted]

Your response does not reference any record retention times required by the firm for [redacted] records.

This letter is not intended to be an all inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations.

The specific violations noted in this letter and the form FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

Given the serious nature of these violations of the Act, all devices manufactured by Helmut Zeph Medizintechnik Gmbh, Obere Hauptstrasse 16-20, 78606 Seitingen, Germany, may be detained upon entry into the United States without physical examination until these violations are corrected.

In order to remove the devices from detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that your response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, the implementation of your

corrections has been verified, your products may resume entry into this country.

Please notify this office, in writing, within 15 working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. If documentation is not in English, please provide a translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement I, General Surgery Devices Branch, HFZ-323, 2098 Gaither Road, Rockville, MD 20850, to the attention of Mr. Joseph L. Salyer.

Sincerely yours,

for Jerry R. Kirk

Lillian J. Gill,
Director
Office of Compliance
Center for Devices and
Radiological Health